Plasma Proteins

Objectives

Should be able to;

list the different types of plasma proteins

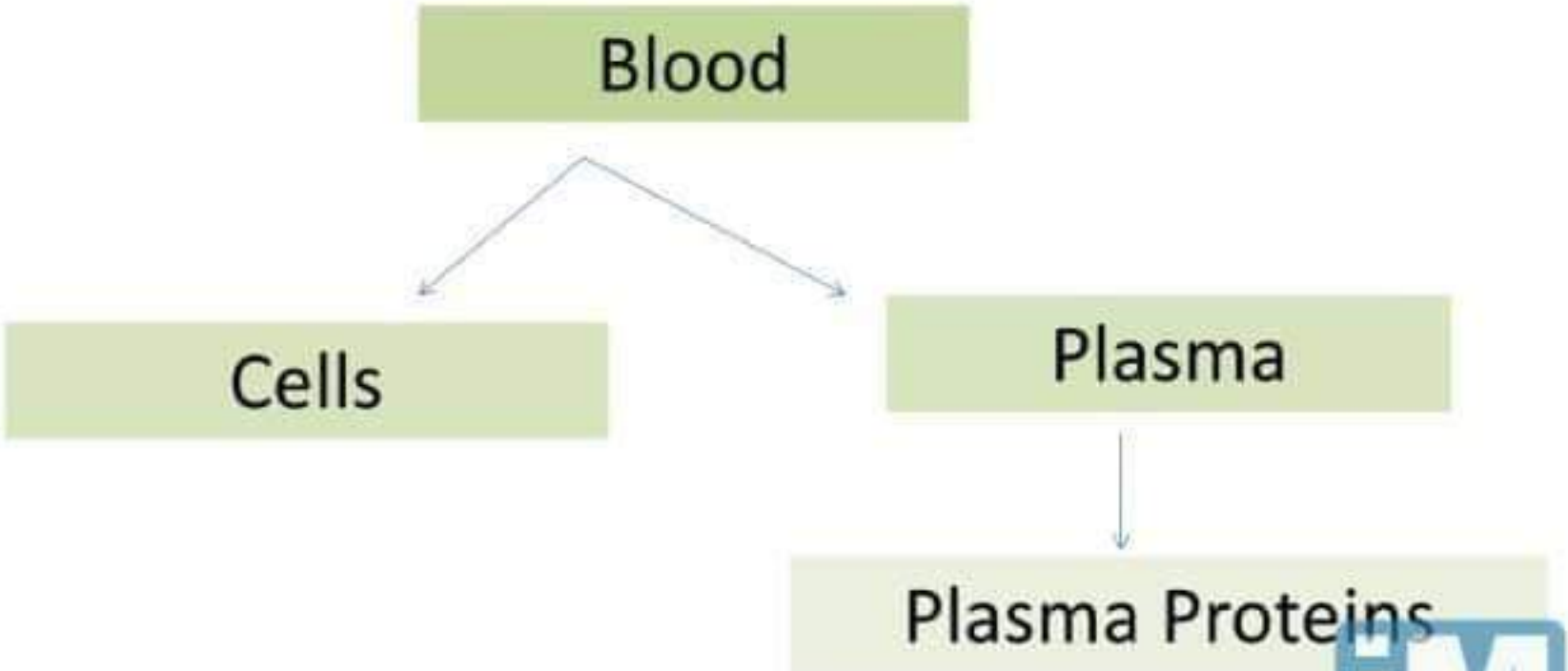
state the basic properties of each

explain the main functions of each

draw, label and interpret the normal electrophoretic pattern

draw, label and interpret the electrophoretic patterns in some given diseases

Plasma proteins



Plasma proteins

- Total plasma protein concentration – 7 – 7.5 g/dL

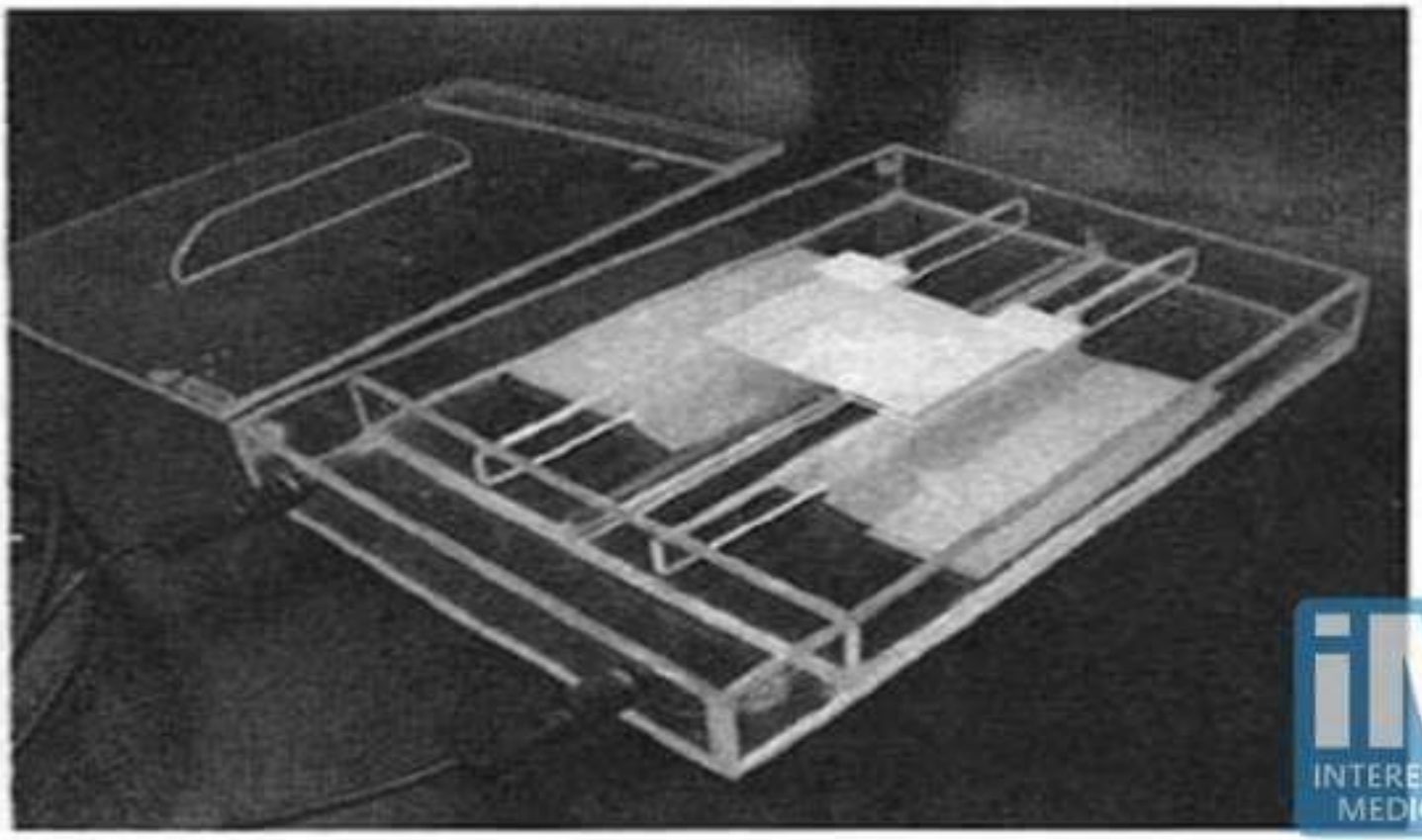
- Complex mixture of proteins
  - proteins
  - glycoproteins
  - lipoproteins
  - antibodies

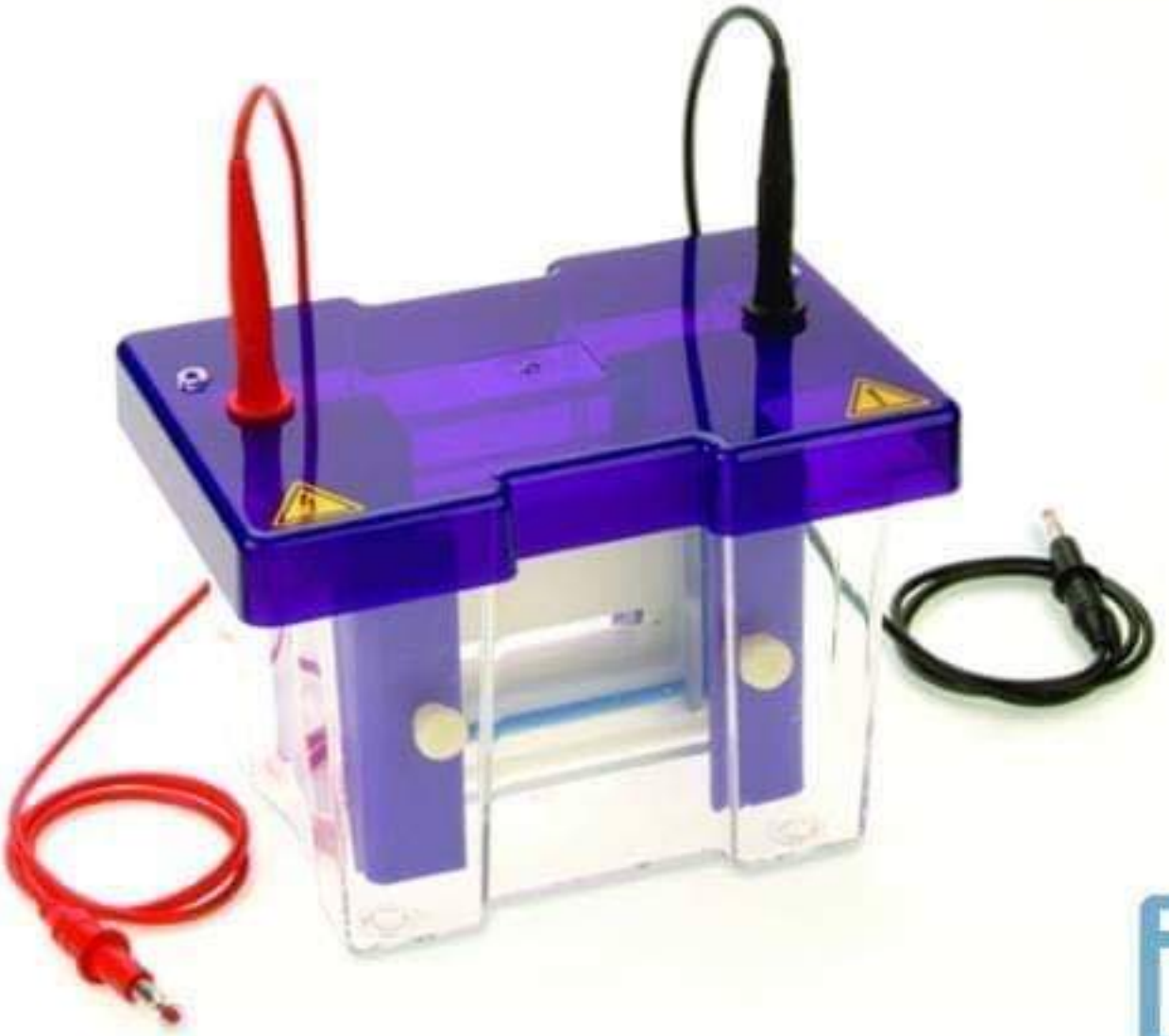
Separation of plasma proteins

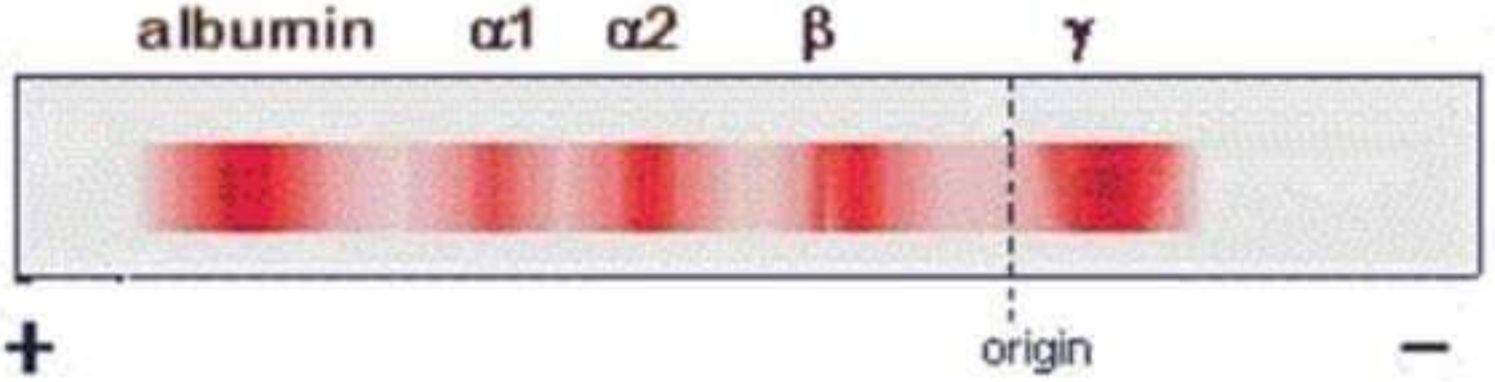
- Separates using solvents and or electrolytes
- According to their solubility characteristics
  - salting out methods
- Can separate plasma proteins into 3 main groups
  - fibrinogen
  - albumin
  - globulin

Plasma protein electrophoresis

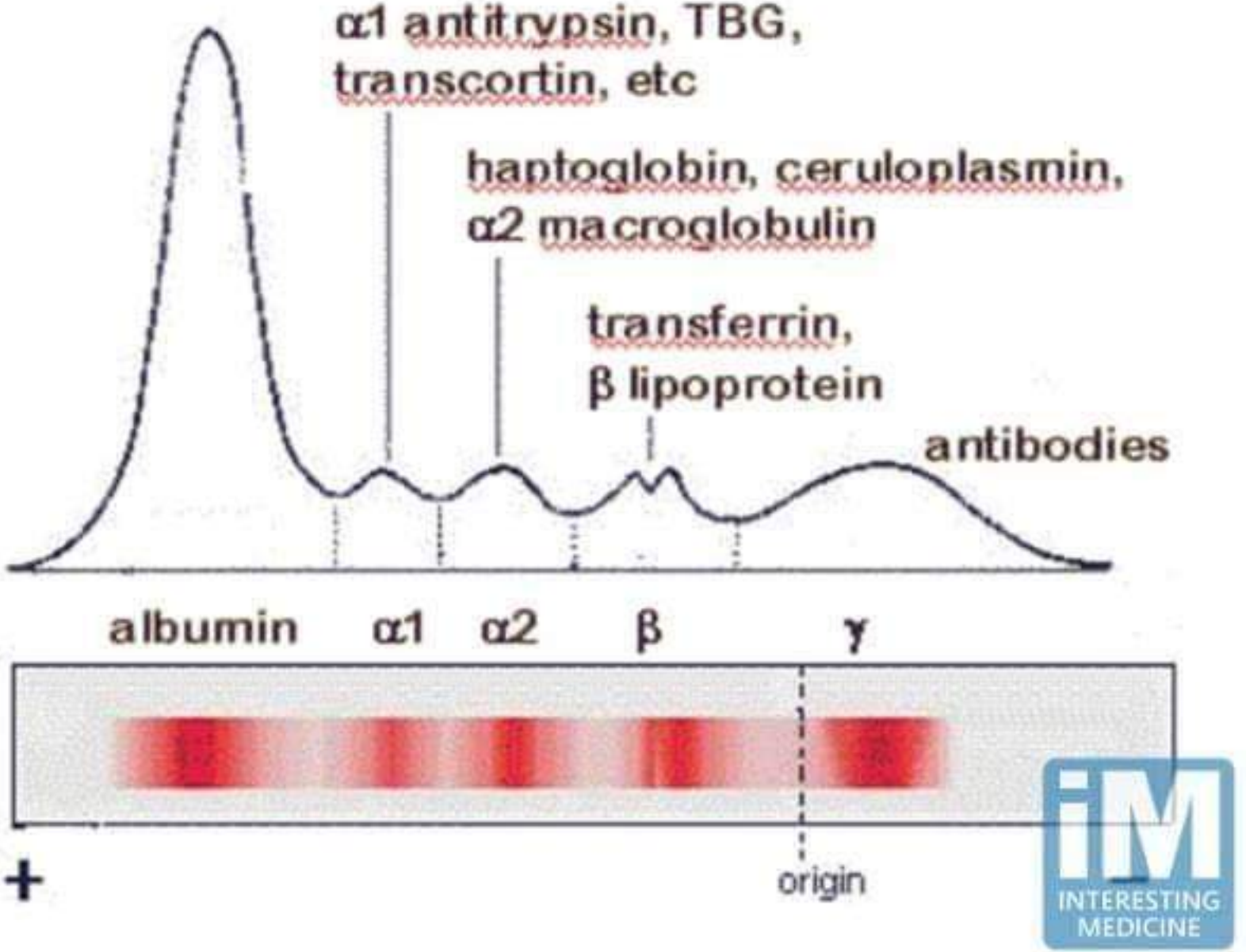
- Supporting medium – cellulose acetate




iM
INTERESTING
MEDICINE



Electrophoretogram


α1 antitrypsin, TBG,
transcortin, etc
haptoglobin, ceruloplasmin,
α2 macroglobulin
transferrin,
β lipoprotein
antibodies
albumin
α1
α2
β
γ
+
origin

1. Albumin (69kDa)

- Major plasma protein
- 3.4 – 4.7 g/dL (60%)
- $T_{1/2}$ – 20 days
- Synthesized in the liver (12g/day)
  as preproalbumin

Functions

1. Maintain plasma oncotic pressure (75 – 80%)

2. Binds various ligands
   - free fatty acids
   - calcium
   - steroid hormones
   - bilirubin
   - copper
   - drugs

3. A negative acute phase reactant

Acute phase proteins

Serum levels of certain proteins change during the acute-phase response

proteins that increase - positive acute phase proteins

proteins that decline - negative acute-phase proteins

(By definition, an acute-phase protein changes by at least 25% during inflammation)

2. α_1 globulin band

a. α_1 antitrypsin

b. α lipoprotein

c. Thyroxin Binding Globulin (TBG)

a. α_1 Antitrypsin (α_1 Antiprotenase)

- 52kDa
- A glycoprotein
- Synthesized by hepatocytes and macrophages
- Principal ***serine protease inhibitor*** (elastase, trypsin)

Functions

1. Inactivate proteases

Important in lungs

A methionine residue is important in the action

2. A positive acute phase reactant

Function in Lungs

Active elastase + α_1 AT ⟶ Inactive elastase

↓

No proteolysis in lungs

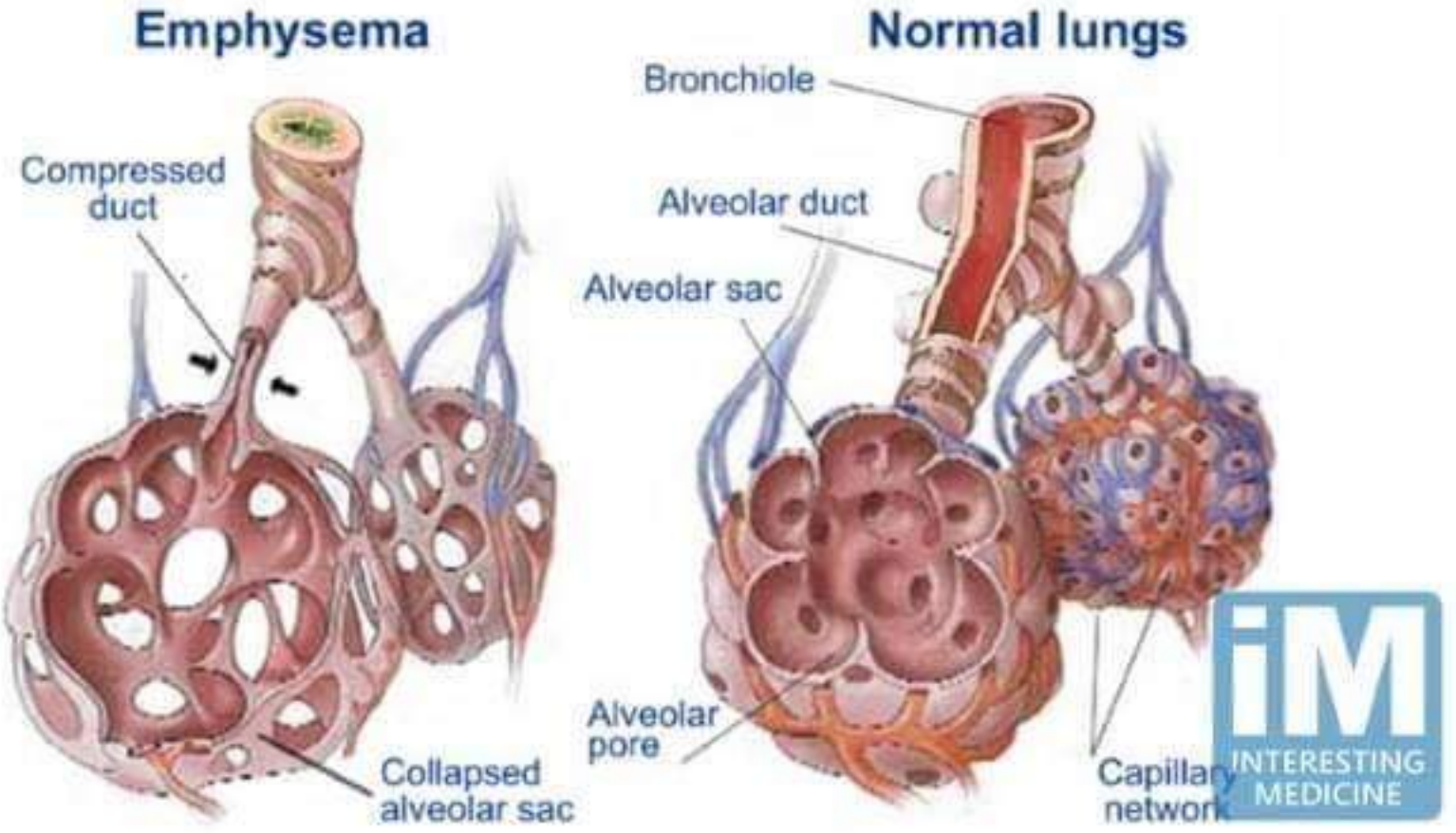
↓

No tissue damage

Deficiency causes lung tissue damage

↓

emphysema



Causes for α_1 AT deficiency

- Inherited (ZZ genotype)
- Smoking

  oxidized methionine to methionine sulfoxide

  ↓

  Inactivates α_1 AT
- α_1 AT deficiency liver disease

c. Thyroid binding globulin

- 54 kDa – a glycoprotein
- Synthesized in the liver
- Binds thyroid hormone in circulation
  carries majority of T_4 in blood
- A negative acute phase reactant

3. α_2 globulin band

a. Haptoglobin

b. Ceruloplasmin

c. Pre-beta lipoprotein

a. Haptoglobin

- 90 kDa
- A glycoprotein
- Synthesized in the liver

Functions

1. Binds extracorpuscular Hb

a tight noncovalent complex

Hb – Hp a large complex
prevents loss of free Hb into the kidney

$T_{1/2}$ – Hp – 5 days

$T_{1/2}$ – Hb – Hp – 90 minutes (rapidly removed by hepatocyes)

Functions

2. A positive acute phase reactant

b. Ceruloplasmin

- 160 kDa
- A glycoprotein
- Bluish in colour
- Synthesized in the liver

Functions

1. Carries 90% of plasma Cu
   each molecule binds 6 atoms of Cu tightly
   Cu is not readily exchangeable

(remaining 10% by albumin – less tightly bound Cu)

2. Cu dependent oxidase activity

3. A positive acute phase reactant

4. β globulin band

a. Transferrin

b. C-Reactive protein

c. ß Lipoprotein

d. Complement Factors

a. Transferrin

- 76 kDa
- A glycoprotein
- Synthesized in the liver
- $T_{1/2}$ – 8 -10 days

Functions

1. Plasma iron transporter

   2mol of Fe^{+3} per mole of transferrin

2. Directs iron to sites where it is required

   (receptor mediated endocytosis)

3. A negative acute phase reactant

a. Transferrin

- Decreased in
  - Iron overload
  - inflammation
  - protein malnutrition

- Increased in
  - iron deficiency anaemia

b. C- Reactive Protein (CRP)

- 25 kDa
- $T_{1/2}$ – 18 -19 hrs (constant)
- Synthesized in the liver
  triggered by inflammatory markers

Functions

- Binds to *phosphocholine* expressed on ,

  dead or dying cells - **activates the complement system**

  microbes and damaged cells – **enhances phagocytosis by macrophages**

  A positive acute phase reactant

Functions

In acute phase response

rapidly increased within 2 hours

reached a peak value in 48 hours

rapid clearance during recovery ($T_{1/2}$ – 18 -19 hrs)

γ globulin band - Immunoglobulins

- Immunoglobulin - Ig
- Important in body's defense mechanisms
- Synthesized by *B lymphocytes* (plasma cells)
  humoral immunity

Basic structure of an Immunoglobulin molecule

- Two identical light (L) chains (23 kDa)
- Two identical heavy (H) chains (53 – 75 kDa)
- Held together as a tetramer by disulfied bonds

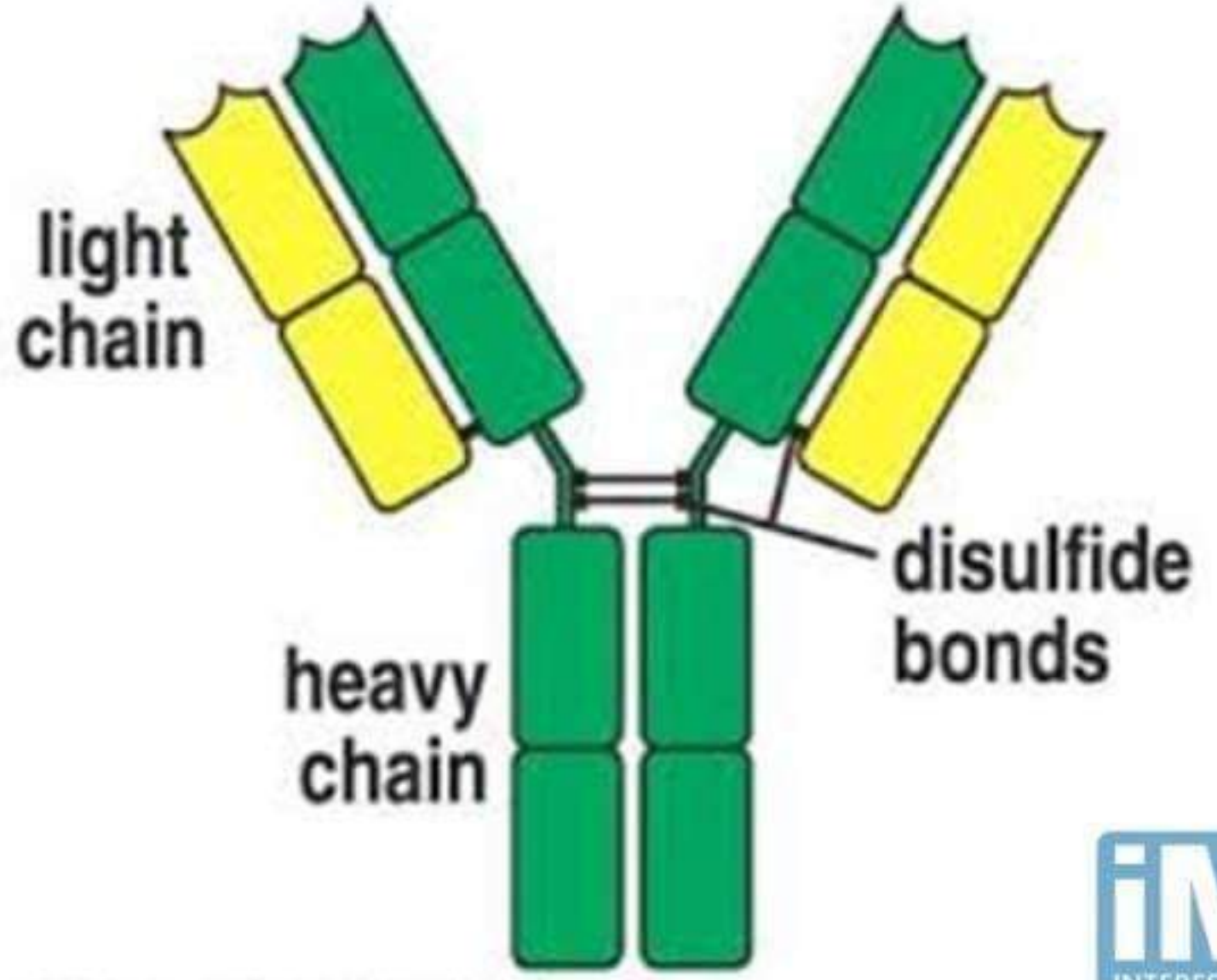
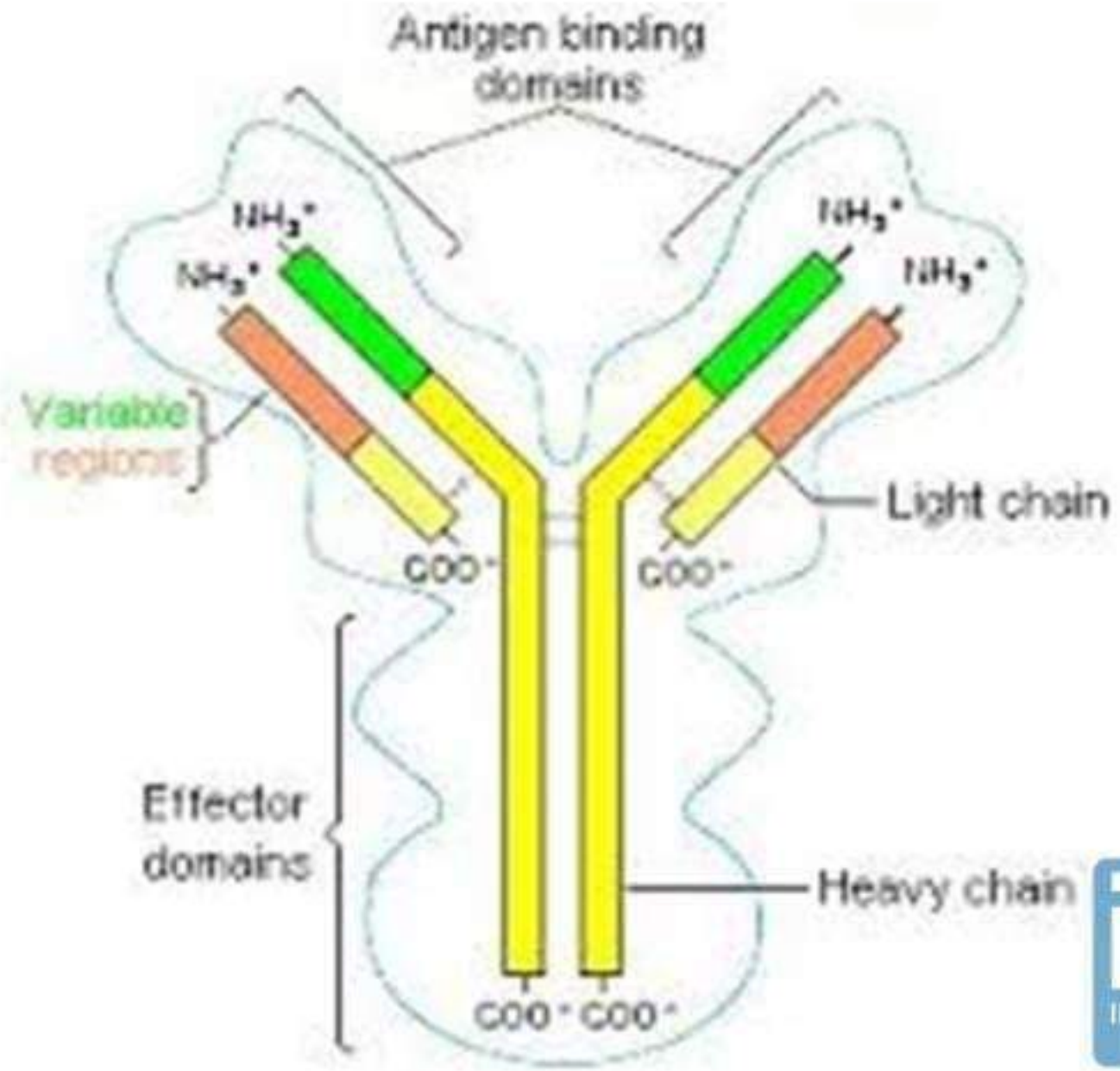
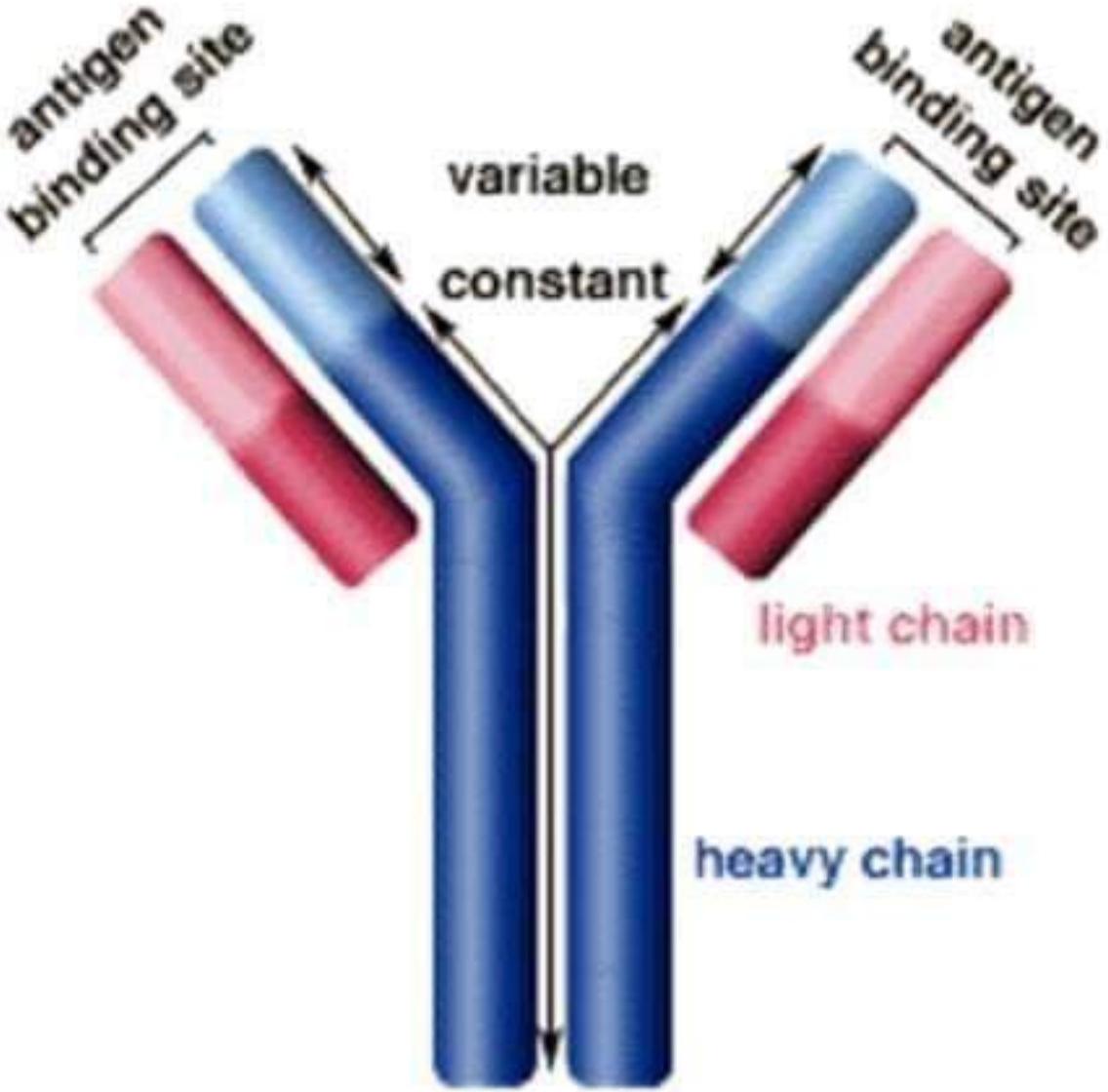


Figure 3-2 Immunobiology 4/e, (© Garland Science 2000)

Light chains

- Two types
  - Kappa (Ϗ)
  - Lamda (л)
- Structural differences in the C_L region
- One Ig molecule contains two Ϗ or л light chains

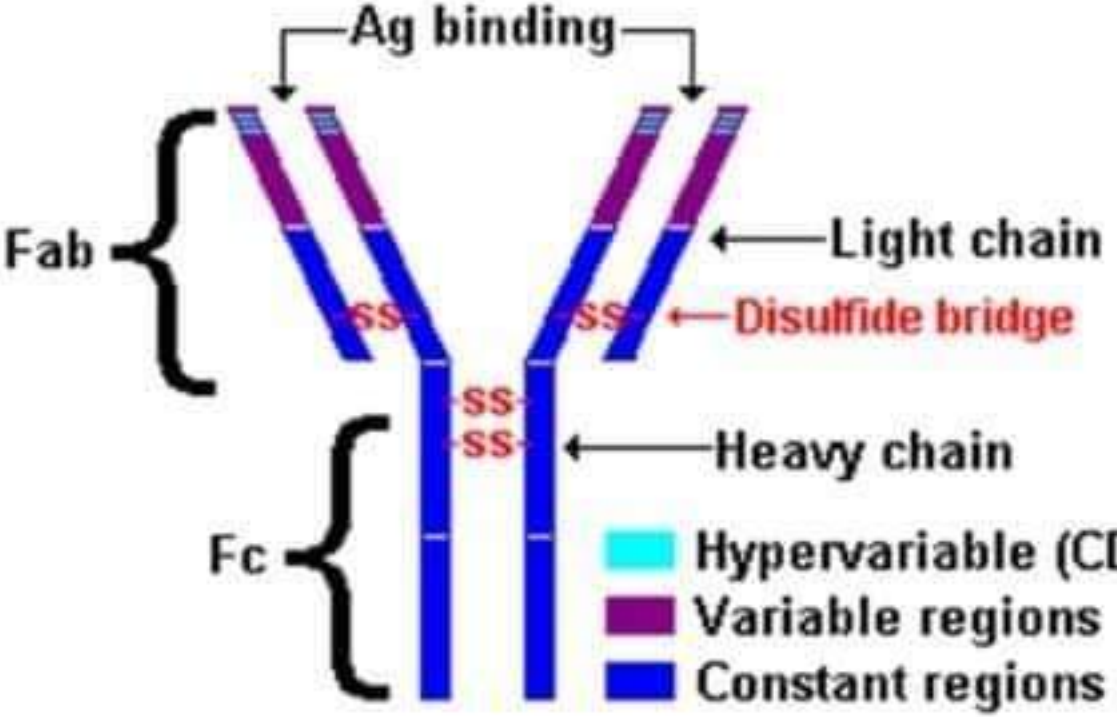

Antigen binding domains
NH_3^+
NH_3^+
NH_3^+
NH_3^+
Variable regions
Light chain
COO^-
COO^-
Effector domains
Heavy chain
COO^- COO^-



Variable region

Hyper-variable region

Constant region



Variable region

- Composed of V_L and V_H domains
- No two variable regions are identical
- Has

  relatively invariable regions

  hypervariable regions (V_L – 3, V_H - 4)

Hypervariable regions

- Also known as *Complementary – determining regions* (CDRs)

  Comprise the Ag binding sites

  Dictate the amazing specificity of Abs

- Surrounding polypeptide regions known as *framework regions*